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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/247,886	02/10/1999	JUHA PUNNONEN	18097-030200	8163

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 10/07/2003 34

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/247,886	PUNNONEN ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-13, 17-23 and 51-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-13,17-23 and 51-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' amendment filed 7-31-03 has been entered. Claims 2, 3 and 8 have been amended. Claims 2-13, 17-23 and 51-64 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 18-23, 51-58 and 64 remain rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See M.E.P.. § 2172.01. The omitted steps are: how to determine whether the recombinant cell-specific binding moiety polypeptide has enhanced ability to bind to the target cell, what is the control that is compared to determine enhanced ability to bind the target cell and is repeated for the reasons set forth in the preceding Official action mailed 2-26-03 (Paper No. 30). Applicant's arguments filed 7-31-03 have been fully considered but they are not persuasive.

Applicants reiterate steps (1) to (5) of claim 18 and argue that step (1) specifies each of the first and second forms of the nucleic acid comprises a polynucleotide encoding a binding moiety polypeptide of an enterotoxin and the resultant recombinant cell-specific binding moiety polypeptide is compared with a particular binding moiety polypeptide encoded by one of the particular staring nucleic acids (amendment, p. 10, 11). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 2-26-03 (Paper No. 30). Step (1) of claim 18 is directed to using nucleic acids to establish a **library of nucleic acids** but no binding moiety polypeptides are expressed in step (1). Step (5) of claim 18 specifies comparison of

binding activity of recombinant cell-specific binding moiety polypeptide with a **binding moiety polypeptide of (1),** however, there is no binding moiety polypeptide expressed in step (1). It is unclear how to compare binding ability of a recombinant cell-specific binding moiety polypeptide with a polypeptide that does not exist in step (1). Further, the recombinant cell-specific binding moiety polypeptides come from the expression of library of the recombinant nucleic acids in step (1). Comparison of the resultant recombinant cell-specific binding moiety polypeptides with the binding moiety polypeptides encoded by the recombinant nucleic acids of step (1) is like comparing to oneself. It is unclear how one could obtain a recombinant cell-specific binding moiety polypeptide with enhanced binding ability by comparing to oneself. Thus, claims 18-23, 51-58 and 64 remain rejected under 35 U.S.C. 112 second paragraph.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 2-13, 17-23 and 51-64 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for obtaining a recombinant cell-specific binding moiety for an ability to increase uptake or specificity of a genetic vaccine for a target cell by recombining nucleic acids in vitro and determining the enhanced binding ability of the recombinant cell-specific binding moiety polypeptide in vitro, does not reasonably provide enablement for a method for obtaining a recombinant cell-specific binding moiety for an ability to increase uptake or specificity of a genetic vaccine for a target cell by recombining nucleic

acids in vivo and determining the enhanced binding ability of the recombinant cell-specific binding moiety polypeptide in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicant's arguments filed 7-31-03 have been fully considered but they are not persuasive.

Applicants argue that the recombinant binding moiety-vector complex can contact target cells in vivo via injection into animal tissues and the cells can be collected from animal for analysis of the presence of the vector via PCR techniques, selectable markers or other molecules of interest (amendment, p. 16, 17). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 2-26-03 (Paper No. 30). The claims are drawn to infecting various types of cells in vivo via various administration routes. The claims read on gene transfer in vivo via various administration routes including parenteral administration, such as intravenous, subcutaneous, intramuscular, or intramedullar injection, and oral administration. The specification fails to provide adequate guidance and evidence how intravenous injection of the library of recombinant nucleic acids can reach various organs, such as brain or kidney, other than liver in vivo, how intramuscular injection of the library of recombinant nucleic acids can reach various organs or tissues, such as brain, heart, or intestine etc., and how oral administration of the library of recombinant nucleic acids can reach various organs, such as skeletal muscle, lung or kedney etc. As discussed in the preceding Official action mailed 2-26-03 (Paper No. 30), the fate of the DNA vector itself, the *in vivo* consequences of altered gene expression, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, and the rate of degradation of the DNA, the level of mRNA produced,

the stability of the mRNA produced, the amount and stability of the protein produced, and the administration routes are all important factors for a successful gene transfer *in vivo*. Absent sufficient gene transfer in the target cells via various administration routes, one skilled in the art would not know how to determine whether a recombinant cell-specific binding moiety polypeptide has enhanced ability in binding to target cells. Further, the specification only teaches detecting the cells taking up the vector of interest and determining the binding activity of the recombinant cell-specific moiety polypeptide in vitro via selectable markers, antigen or PCR techniques but the specification fails to provide adequate guidance how to determine the enhanced binding ability of a recombinant cell-specific binding moiety polypeptide in vivo. Therefore, the specification fails to provide sufficient enabling disclosure for the full scope of the invention claimed.

Applicants argue that the claimed methods are simply directed to obtaining recombinant cell-specific binding moiety having increased uptake or specificity of a vaccine vector for a target cell and the recombination and screening procedures have been disclosed. Applicants further argue that the factors cited by examiner for gene transfer in vivo do not pertain to successful practice of the claimed methods and the recombinant cell-specific binding moieties that do not bind to target cells, not properly expressed or degraded are merely excluded from further analysis and the unpredictable aspects that may apply to gene therapy in vivo are not relevant to the present invention (amendment, p. 17-19). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 2-26-03 (Paper No. 30) and the reasons set forth above.

Conclusion

No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.